REMARKS/ARGUMENTS

Claims 1, 15-17, 22 and 51-59 are pending. Independent Claim 1 has been directed to the previously elected subject matter of SEQ ID NO: 2. Claims 16 and 17, which had been withdrawn as being directed to non-elected species, have been amended to facilitate their rejoinder. New Claims 51-59 find support in the original claims. Accordingly, the Applicants do not believe that any new matter has been added.

The Applicants thank Examiners Wegert and Andres for the courteous and helpful interview of November 15, 2005. The Applicants were requested to elaborate on the applicability of the rat animal model to determination of the effects of pharmacological compounds in humans and were encouraged to provide data showing that SMR1 peptides have activity in humans or the human homologs of SMR1 exist.

To address a scope of enablement rejection regarding mode of administration, the Applicants were encourage to submit data that non-parenteral modes of administration would be efficacious, or to limit the mode of administration to parenteral administration, since parenteral administration was exemplified in the disclosure.

The Applicants urged that the terms "impaired social activity" "related to sexuality" would not only be understood by those with skill in the art, but were actually exemplified by the experimental data in the specification. The Examiners agreed to reconsider this indefiniteness rejection in view of these arguments and data.

Restriction/Election

The Applicants previously elected Group I, Claims 1-20 and 22, directed to methods for treating a disease using a ligand, and the species of SEQ ID NO: 2 (Gln His Asn Pro Arg) and the species "impaired social activity linked to sexuality". The Restriction Requirement has now been made FINAL.

Oath/Declaration

The oath/declaration was objected to as containing non-initialed alterations. 37 C.F.R. 1.52(c) refers to alterations made to the application papers (e.g., the specification and original claims) after the signing of the oath, but does not refer to alterations made to the oath at the time of signing. While the wording of an oath or declaration cannot be amended, altered or changed in any manner after it has been signed (see MPEP 602.01), the correspondence address on the present oath was corrected at the time the oath was signed, not afterward. Accordingly, the Applicants respectfully request that this objection be withdrawn.

Claim—Objection

Claim 2 was objected to as containing non-elected subject matter. This objection is moot in view of the amendments above. New Claim 59 is broadly directed to treatment of mental diseases. The Applicants respectfully request that this claim be examined to the extent that it reads on the elected species.

Rejection—35 U.S.C. §112, second paragraph

Claims 1 and 15 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for using the terms "impaired social activity" and "linked to sexuality". The term "impaired social activity linked to sexuality" is defined in the specification page 14, lines 13-16, as an impairment of social relationship to a sexual partner.

Moreover, one skilled in the psychiatric or psychological arts would readily understand the meaning of these terms. To further establish that these terms are well-known in the art, the Applicants attach herewith portions of DSM IV. Page 496, second paragraph,

of DSM-IV states that "a personality disorder may coexist with a sexual disfunction" and establishes a link between a disturbance of sexual functioning and relational problems.

Furthermore, the summary of diagnostic criteria for hypoactive sexual desire disorder (page 498) indicates that "the disturbance cause marked distress or interpersonal difficulty". This same association is established on pages 500 and 504 between sexual aversion disorder and male erectile disorder, respectively, together with marked distress and interpersonal difficulty. Moreover, as shown by Yoo et al., Benassi-Benelli et al. and Islam et al., which were submitted with the prior response, these sexual and social behaviors are well-known and characterized in the art. Therefore, the Applicants respectfully submit that one with skill in the relevant art would understand the meaning of "impaired social activity" and "linked to sexuality" and request that this rejection be withdrawn.

Rejection—35 U.S.C. §112, first paragraph

Claims 1, 2, 15, 20 and 22 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement.

One concern discussed in the interview was that the QHNPR peptide was first identified in rats and that a rat derived peptide would not be expected to be active in humans. As shown in the Declaration of Dr. Rougeot (attached) the QHNPR (SEQ ID NO: 2) peptide has the same receptor in rats and in humans: NEP (neutral endopeptidase, also known as neprilysin). NEP is a peptidase that degrades substance P. Substance P is involved in sexual behavior (see the abstract of Argiolas, "Neuropeptides and sexual behavior, attached).

The QHNPR (SEQ ID NO: 2) peptide inhibits NEP (neprilysin) in rats and humans, see Rougeot et al., PNAS, 2003, attached. While the invention is not intended to be limited to a particular mechanism of action, the inhibition of NEP would be expected to reduce the degradation of substance P, thus increasing the levels of substance P available to modulate

sexual behavior. In fact, Fig. 1 of the attached Declaration of Dr. Rougeot show just that: that the QHNPR (SEQ ID NO: 2) peptide inhibits the breakdown of substance P by human NEP. These experimental data show that the peptide of SEQ ID NO: 2 is active in humans and regulates molecules such as substance P involved in sexual behavior.

Another concern was that the type of disorder treated by the administration of the QHNPR (SEQ ID NO: 2) peptide was not adequately described or enabled. The term "impaired social activity linked to sexuality" is discussed above in regard to the indefiniteness rejection. With respect to enablement, methods of using an SMR1 peptide (e.g., SEQ ID NO: 2) to treat social and sexual dysfunctions in mammals are not only described by the specification, they are extensively exemplified. The disclosure exemplifies many such behaviors, including increased interest in the environment, capacity for arousal and vocalization (page 18, lines 15-20), increased social and interpersonal activities (page 19, lines 20-22), as well as many other behaviors related to social activity and sexuality which are exemplified by the data in Examples 2-9. Examples 2 to 9 describe a panel of behaviour modifications following administration of QHNPR peptide (SEQ ID NO: 2) in rats, e.g. increased interest in environment and capacity for arousal (example 2), increased behaviour of the males in the presence of females (example 3), social interaction and interpersonal activities before sexual intercourse (example 4), decreased fear of partner and increased ability to relate (example 5), loss of avoidance symptoms and enhanced willingness to enter into relationship (example 6) and prolongated social intercourse signs towards female and attention signs to personal toilet (example 7). The specification demonstrates that peptide SEQ ID No: 2 improved a panel of sexual behaviours in rat. Impaired social activity linked to sexuality is defined in the specification as the impairment of social relationship to a sexual partner (page 14, lines 13-16). Examples 3 through 7 clearly indicate that treatment of male rodents with an SMR1 peptide improves their sexual behavior.

Animal Models. The use of animal models, such as that rat models exemplified in the specification, to model human psychological behavior has long been an integral part of medical and scientific research; see the previously attached Declaration/Affidavit of Dr. Renoncet-Ungeheuer. Accordingly, the Applicants respectfully request that this rejection be withdrawn as the Applicants clearly exemplify the effects of the administration of SMR1 peptides on mammalian social and sexual behavior. The Applicants acknowledge the Examiner's concern with establishing the validity of an animal model, however, the models disclosed in the specification are those accepted within the art and the attached Declaration of Dr. Rougeot further provides a nexus between the animal models and treatment of humans by showing that the QHNPR peptide (SEQ ID NO: 2) inhibits the breakdown of substance P in human cells (Fig. 1 of Declaration). While the claims are not directed to a particular mechanism of action, since substance P is involved in sexual behavior, one with skill in the art would reasonably expect that the QHNPR peptide would modulate human sexual behavior by increasing substance P levels.

Route of Administration. Another enablement concern was that the specification did not enable different routes of administration for an SMR1 peptide like that of SEQ ID NO: 2. For example, that oral administration of such a peptide would be ineffective since it could be digested prior to exerting its biological effect. However, it is now recognized in the pharmacological arts that peptides, including the insulin peptide, may be administered by other routes such as orally and nasally or targeted for delivery via the gastrointestinal tract, see e.g., Frasno, "Innovative strategies for the oral delivery of drugs and peptides", Pontiroli, "Peptide hormones: Review of current and emerging uses by nasal delivery", and Leopold, ""Targeted delivery' in the gastrointestinal tract". Thus, while the specification exemplifies that acute venous peripheral administration is an effective route of administration for peptide SEQ ID NO: 2, the Applicants respectfully submit that administration of this peptide by other

routes, including the oral route, would be within the skill of one in the pharmacological arts. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejections—35 U.S.C. §112, first paragraph

Claims 1, 2, 15, 20 and 22 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate description. Treatment of humans in subsumed into the original claims (see Claim 1) which are directed to treatment of mammals. Page 7, lines 16-17 of the specification specifically indicates that "mammals" includes humans. While treatment of humans is not exemplified in the disclosure, this is not required for adequate description (the enablement issues associated with treatment of humans are discussed above). Therefore, the original disclosure contemplates and discloses the treatment of mental diseases in humans using SMR1 peptides. The elected species to which examination is presently directed (impaired social activity linked to sexuality) is disclosed by page 16, line 26 of the specification and by Claim 15. Page 15, lines 5-15 and Claim 22 describe various routes of administration as well as dosages of the SMR1 peptides. Therefore, this subject matter is also described by the original disclosure. Accordingly, the Applicants respectfully submit that this rejection may be withdrawn.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application as directed to the elected species is now in condition for allowance. Thus, extension of examination to additional species and subsequent allowance of this application is earnestly requested.

Respectfully submitted,

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